REMARKS

In this Amendment, Applicant has amended Claims 1 – 7 to specify different embodiments of the present invention and overcome the rejection. It is respectfully submitted that no new matter has been introduced by the amended claims. All claims are now present for examination and favorable reconsideration is respectfully requested in view of the preceding amendments and the following comments.

REJECTIONS UNDER 35 U.S.C. § 101:

Claims 3 and 6 have been rejected under 35 U.S.C. § 101 as allegedly failing to define a patentable subject matter.

It is respectfully submitted that in view of the amendments to Claims 3 and 6, the rejection has been overcome. More specifically, Claims 3 and 6 have been amended to recite the step of "administering the glycoprotein to a subject as a medicinal agent."

Therefore, the rejection under 35 U.S.C. § 101 has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 101 is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112 FIRST PARAPGRAPH:

Claims 1 – 6 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains to make and use the invention.

It is respectfully submitted that in view of the present amendments to the Claims 1 – 6 and the enclosed experiments results, the rejection has been overcome. In particular, the Examiner admitted that the specification being enabled for glycoproteins from blood serum, liver, thymus or eye, which is the subject matter claimed in Claims 4 – 6 (see

descriptions of Examples 3 on page 13, Example 12 on page 26 and Example 17 on page 26 about glycoprotein from eyes; Example 4 on page 13 about glycoprotein from livers; Example 5 of page 14 about glycoprotein from livers; and Example 6 of page 15 about glycoprotein from thymus). Therefore, it is incorrect to reject Claims 4 – 6 as not being enabled by the specification. In addition, Applicant respectfully submitted that the claimed glycoprotein, pharmaceutical composition and method of use are sufficiently supported by the descriptions in the specification, such as Examples 1 – 17 of the specification. These examples specify the steps need to be taken to make and use the glycoprotein as presently claimed. In addition, enclosed please find additional experiments performed on different organs by the skilled artisan according to the steps of originally disclosed specification (see attachment). It is respectfully submitted that a person skilled in the art will can make and use the present invention as disclosed.

Therefore, the rejection under 35 U.S.C. § 112, first paragraph has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 112 SECOND PARAPGRAPH:

Claims 1 – 6 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is respectfully submitted that the amended Claims 1 – 6 clearly point out and define the embodiment of the present invention. More specifically, Claims 3 and 6 have been amended to recite specific steps. "Glycoproteins" in Claims 1, 4 and 7 have been amended to "a glycoprotein." "[W]ith the help of" in Claims 1 and 7 has been amended to "using." "Pharmaceutical composition, including" in Claims 2 and 5 has been amended to "A pharmaceutical composition comprising." Claim 4 has been rewritten to independent form. Claims 2, 3, 5 and 6 have also amended to add "the" in front of "glycoprotein."

Therefore, the rejection under 35 U.S.C. § 112, second paragraph, has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested.

REJECTIONS UNDER 35 U.S.C. §102 and §103:

Claims 1 –6 have been rejected under 35 U.S.C. §102 and §103 as allegedly being anticipated or unpatentable over Karler et al. (US 4,169,139), hereinafter Karler.

Applicant traverses the rejection and respectfully submits that the embodiments of present-claimed invention are not anticipated by or obvious over Karler. It is respectfully submitted that there are significant differences between the embodiments of the present invention and the disclosure in Karler.

As disclosed in Karler, glycoproteins isolated according to Karler are produced by initial autolysis of tissue of different organs. Karler indicates that the tissue is homogenised and the homogenate is mixed to separation for 24 hours. In tissue homogenisation, cell walls are destroyed and a great amount of intracellular enzymes enters in the solution, which will decompose proteins and glycoproteins present in the solution. The degree of destruction depends on the time of contact between decomposed components and enzymes. During 24 hours, a very significant amount of protein and glycoprotein destruction occurs. Applicant respectfully submits that, when selecting the method of isolating glycoproteins, the inventors of the present inventions tried various isolation methods. But the investigations have shown, enzymes produced in destroying cell walls partially destroy glycoproteins and when isolating glycoproteins according to this method, Applicant was not able to produce any glycoproteins having biological activity in super-small doses.

To the contrary, according to the disclosure of the present invention, Applicant successfully obtained glycoproteins isolated from an intercellular space of tissues (intercellular matrix) of different organs. This feature is one of distinctive features in our invention. It is apparent from the specification that in isolating glycoproteins, the

tissue is not homogenised but cut into rather large pieces (or even is not cut but incised in the case when the organ is small), and is additionally washed to remove damaged cells and to wash off intracellular enzymes released from the damaged cells. Thus, Applicant prevents intracellular component from entering the extract. It is precisely glycoproteins from the intercellular matrix that enter the extract. Due to the absence in the extract of intracellular enzymes, glycoproteins, in Applicant's opinion, are not subject to enzymic destruction when being isolated. Therefore, the embodiments of the present invention as claimed are different from the disclosures in Karler. Without motivation or reasonable expectation of success, a person of ordinary skill in the art will not modify Karler to achieve the present invention as claimed.

Therefore, the rejection under 35 U.S.C. §103, second paragraph, has been overcome. Accordingly, withdrawal of the rejections under 35 U.S.C. §103 is respectfully requested.

Having overcome all outstanding grounds of rejection, the application is now in condition for allowance, and prompt action toward that end is respectfully solicited.

Respectfully submitted,

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By _____
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Enclosure:

Additional Examples 1 – 16 showing enablement of the present invention

Examples 1 – 16 showing enablement of the present invention:

Example 1. Glycoproteins from rat heart

Experiments were conducted on Wistar line rats of both sexes, weighing 150-180 g. The animals were decapitated, the heart was cut out, carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$), several deep incisions were made with a scalpel on the heart, followed by repeated washing in the salt solution and extracting in the solution of the above composition at the temperature of 4°C for 2 hours (3-4 ml of the extracting solution per 1 heart). The resultant extract was collected. The hearts were poured with a fresh portion of the salt solution and extracted for one more hour. The resultant extracts were combined. To remove blood cells and damaged heart cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified heart glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.1-3).

Example 2. Glycoproteins from cattle heart

Experiments were carried out on hearts of cattle of both sexes. Fresh hearts were obtained from a slaughter-house from just slaughtered animals. On the spot they were carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0/001 mole/litre $CaCl_2$) and placed in a fresh portion of the salt solution. Further, the hearts were cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2

hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The hearts were poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged heart cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectrofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified heart glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.4-6).

Example 3. Glycoproteins from rabbit lung

Experiments were carried out on rabbits of both sexes. The lung was cut out from the rabbits and carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0/001 mole/litre $CaCl_2$), cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The lung tissues were poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged lung cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectrofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure

disclosed in the present specification. All identified lung glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.7-9).

Example 4. Glycoproteins from rat spleen

Experiments were conducted on Wistar line rats of both sexes, weighing 150-180 g. The animals were decapitated, the spleen was cut out, carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$), several incisions were made with a scalpel on the spleen, followed by repeated washing in the salt solution and extracting in the solution of the above composition at the temperature of 4°C for 2 hours (3-4 ml of the extracting solution per 1 spleen). The resultant extract was collected. The spleens were poured with a fresh portion of the salt solution and extracted for one more hour. The resultant extracts were combined. To remove blood cells and damaged spleen cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified spleen glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.10-12).

Example 5. Glycoproteins from cattle kidney

Experiments were carried out on kidneys of cattle of both sexes. Fresh kidneys were obtained from a slaughter-house from just slaughtered animals. On the spot they were carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$) and placed in a fresh portion of the salt solution.

Further, the kidneys were cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The kidneys were poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged kidney cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectrofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified heart glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.13-15).

Example 6. Glycoproteins from cattle mammary gland

Experiments were carried out on mammary glands of young heifers aged up to 2 years. Fresh mammary glands were obtained from a slaughter-house from just slaughtered animals. On the spot they were carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$) and placed in a fresh portion of the salt solution. Further, the mammary glands were cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The mammary glands were poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged mammary gland cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectrofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified mammary gland glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.16-18).

Example 7. Glycoproteins from cattle ovaries

Experiments were carried out on ovaries of young heifers aged up to 2 years. Fresh ovaries were obtained from a slaughter-house from just slaughtered animals. On the spot they were carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$) and placed in a fresh portion of the salt solution. Further, the ovaries were cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The ovaries were poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged ovary cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectrofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified ovary glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.19-21).

Example 8. Glycoproteins from rabbit brain

Experiments were carried out on rabbits of both sexes. The brain was extracted from the rabbits, carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0/001 mole/litre $CaCl_2$), cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The brain tissues were poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged brain cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectrofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified brain glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.22-24).

Example 9. Glycoproteins from rat marrow

Experiments were conducted on Wistar line rats of both sexes, weighing 150-180 g. The animals were decapitated, large bones were extracted, crushed and the marrow was extracted, carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$), and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1.5-2 g of the marrow). The resultant extract was collected. The marrow tissues were poured with a fresh portion of the salt solution and extracted for one more hour. The resultant extracts were combined. To remove blood cells and damaged marrow cells, the

tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified marrow glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.25-27).

Example 10. Glycoproteins from pig pancreas

Experiments were carried out on pancreas of pigs of both sexes. Fresh pancreas was obtained from a slaughter-house from just slaughtered animals. On the spot it was carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$) and placed in a fresh portion of the salt solution. Further, the pancreas was cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The pancreas was poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged pancreas cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified pancreas glycoproteins exhibited

biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.28-30).

Example 11. Glycoproteins from rat thyroid gland

Experiments were conducted on Wistar line rats of both sexes, weighing 150-180 g. The animals were decapitated, the thyroid gland was cut out, carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$), several incisions were made on the thyroid gland with a scalpel, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 thyroid gland). The resultant extract was collected. The thyroid glands were poured with a fresh portion of the salt solution and extracted for one more hour. The resultant extracts were combined. To remove blood cells and damaged thyroid gland cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified thyroid gland glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.31-33).

Example 12. Glycoproteins from rat bowels

Experiments were conducted on Wistar line rats of both sexes, weighing 150-180 g. The animals were decapitated, bowels were cut out, carefully cleaned, washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$), cut into fragments with the weight of about 1.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C

for 2 hours (3-4 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The bowel fragments were poured with a fresh portion of the salt solution and extracted for one more hour. The resultant extracts were combined. To remove blood cells and damaged bowel cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified bowel glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.34-36).

Example 13. Glycoproteins from bovine seminal organs

Experiments were carried out on bovine seminal organs. Fresh seminal organs were obtained from a slaughter-house from just slaughtered animals. On the spot they were carefully washed in a physiological salt solution (0.15 mole/litre NaCl; 0.04 mole/litre KCl; 0.001 mole/litre $CaCl_2$) and placed in a fresh portion of the salt solution. Further, the seminal organs were cut into fragments weighing 1.5-2.0 g, again washed in the salt solution and extracted in the solution of the above composition at the temperature of 4°C for 2 hours (4-5 ml of the extracting solution per 1 tissue fragment). The resultant extract was collected. The seminal organs were poured with a fresh portion of the salt solution and extracted for 1 more hour. The resultant extracts were combined. To remove blood cells and damaged seminal organ cells, the tissue extract was centrifuged at 5000 g during 20 minutes, then decanted and used for further purification.

Salting-out and pH-isoelectofocusing of the tissue extract were performed according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified seminal organ glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.37-39).

Example 14. Glycoproteins from cattle bile

To conserved medical bile (registration number 70/529/5; OAO "Samson", St.-Petersburg), during intense stirring, dry sulphuric ammonium was added to form a saturated salt solution (4°C, pH 8.0-8.5). The resultant precipitate of admixture proteins was deposited by centrifuging at 35000 g during 30 minutes, the supernatant was collected and long dialysed against distilled water using a cellulose film of Russian manufacture (GOST 7730-89). During dialysis, distilled water was repeatedly replaced with fresh water. After ammonium ions had been completely removed, the supernatant was concentrated to the volume of 100 ml using evaporation at a rotor evaporator in vacuum at the temperature of 35-40°C and the salting-out procedure was repeated under the same conditions. The second supernatant produced in a similar manner was also dialysed against distilled water to completely remove ammonium ions and then pH-isoelectrofocusing of the dialysed supernatant was perform according to the procedure disclosed in the present specification. After pH-isoelectrofocusing, three protein fractions were collected – acid, with pI in the region of pH 4.6-8.5 and main glycoproteins.

To determine biological activity, effect of the aqueous glycoprotein solution on viscoelastic properties of hepatocyte membranes was studied according to the procedure disclosed in the present specification. All identified bile glycoproteins exhibited biological activity in super-small doses corresponding to concentrations of 10^{-12} – 10^{-29} mole/litre and lower (Figs.40-42).

Example 15. Effect of aqueous solution of acid glycoprotein from the cattle bile in oral administration per particle size of human bile

For investigation a pharmaceutical composition was prepared that was an aqueous solution of acid glycoprotein from cattle bile (hereinafter AGB) in concentration: 10^{-10} g of acid glycoprotein from cattle bile per 1l of water.

Investigation was carried out on voluntaries.

A voluntary L., male, 60 years old.

No complaints made. During ultrasound examination (USE) of the hepatobiliar zone, moderate compression of the gall bladder wall was discovered, homogeneous bile. Features of fat liver dystrophy.

He was administered an aqueous AGB solution in concentration of 10^{-14} Mole/l during 21 days by 100 ml 3 times a day 30 minutes before meal. Bile was produced by duodenal probing.

Portion "B" was investigated – before administering the preparation, in 1, 3, 6, 10, 16, 21 days (intervals between bile collections were made empirically). The bile was investigated by micro-diffusion method.

The average particle size was reduced from 52 nm (control portion – without the preparation) to 17.0 nm by the 16^{th} day of administering the AGB solution and was kept at that level in the 5^{th} probe (by the 21^{st} day). During preparation administration, food ration did not change.

A voluntary K., female, 23 years old.

No complaints made. During USE of the hepatobiliar zone no pathology was revealed. Bile was homogeneous.

She was administered an aqueous AGB solution by 100 ml 3 times a day 30 minutes before meal (food ration did not change). Also bile of portion "B" was investigated produced during duodenal probing: before preparation administration; in 1 day after beginning of preparation administration; in 4 days; in 8 days; in 14 days; in 20 days.

The bile was investigated by micro-diffusion method. The average particle size before the experiment began corresponded to 38.4 nm. Reduction of the particle size was noted on the 8^{th} day after preparation administration and it continued decreasing up to the 20^{th} day, the difference in reducing bile particle radius by the 14^{th} and 20^{th} days being insignificant.

Thus, the particle radius decreased from 38.4 nm at the beginning of investigation to 14.5 nm by the 20th day after preparation administration.

Example 16. Effect of pharmaceutical means based on acid glycoprotein from cattle eye retina on restoration of eye retina function in Campbell line rats predisposed to eye retina dystrophy

For examination, a pharmaceutical composition of the following make-up was prepared:

Acid glycoprotein from eye retina	1.10^{-10} g
Sodium chloride	8.8 g
Calcium chloride	0.001 g
Water	up to 1 l

Investigation was conducted on Campbell line rats genetically predisposed to eye retina dystrophy. A series of experiments were carried out to study the effect of the above pharmaceutical composition on restoration of eye retina function. Wistar line rats were used as a control, without preparation administration, as well as Campbell line rats with administering to them a physiological salt solution.

It is possible to observe development of the pathological process using different investigation methods one of which is a method of determining the relationship of rhodopsin in the ocular cup and, actually in the retina tissue. In healthy animals, this relationship is expressed by a digital parameter the value of which is about 1. This means that rhodopsin is basically localised in exterior photoreceptor segments and all "worked-out" exterior segments are already absorbed by cells of retina pigment epithelium. In animals with hereditary retina dystrophy, the value of this parameter varies in the region of 0.5, which evidences accumulation of debris of exterior segments in the interphotoreceptor space, i.e. the progress of pathological process.

The pharmaceutical means under investigation was administered to young rats by intra-abdominal injections four times by 0.2 ml on the 10th, 20th, 30th and 40th days after birth. Results obtained are presented in *Table 1*. It follows from these data that administering the proposed means promotes improvement of retina function in animals of the genetically unstable line (the D/C index characterising the degree ofdestruction of

exterior photoreceptor segments reached values corresponding to such in a normally functioning retina, i.e. in the Wistar line rats..

Table 1. Effect of the proposed pharmaceutical means on rhodopsin content

Rat line	Average animal weight (g)	Rhodopsin content in cup (mg)	Rhodopsin content in retina (mg)	D/C ratio
A	B	C	D	D/C
Wistar Without administering preparations	75.65	0.062	0.054	0.87
Campbell administering salt solution	44.77	0.040	0.020	0.50
Campbell administering proposed pharmaceutical means	64.13	0.062	0.052	0.84